Selective Monoacetylation of Symmetrical Diols and Selective Monodeacetylation of Symmetrical Diacetates Using HY-Zeolite as Reusable Heterogeneous Catalyst[1]

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Abstract: HY-Zeolite has been found to be an efficient and reusable catalyst for selective monoacetylation of symmetrical diols and selective monodeacetylation of symmetrical diacetates to form the products in high yields.

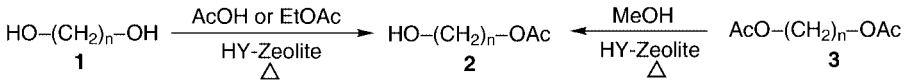
Key words: monoacetylation, symmetrical diols, monodeacetylation, symmetrical diacetates, HY-Zeolite

Selective protection of multiple identical functional groups is very important in organic synthesis. Monoprotected symmetrical diols are suitable starting materials for the preparation of various sex pheromones and medicinally important compounds.[2] The yields of the final products depend on the efficient preparation of these starting materials from the corresponding symmetrical diols. However, hydroxyl groups in similar chemical environments react at similar rates with the protecting reagents often leading to the formation of diprotected products. Thus the functionalization of only one hydroxyl group of a symmetrical diol is not an easy process. Monoprotection of polyols can be achieved by carefully controlled reaction conditions,[3] continuous extraction,[4] the use of solid-supported reagents,[5] alumina,[6] lanthanum halides,[7] phase transfer catalysts[8] and insoluble polymer supports[9] or via the formation of cyclic compounds.[10] However, some of the methods require special experimental set ups, some of the catalysts are not readily available or have to be freshly prepared at the time of use and some of the protocols are not straightforward. The reusability of several catalysts has also not been verified. Hydroxy compounds are frequently protected by acetylation in organic synthesis. Monoacetylated symmetrical diols were prepared earlier for the synthesis of sex pheromones of Lepidoptera by treatment of symmetrical diols with acetic anhydride (Ac_2O) under strongly basic and refluxing conditions.[2b] The yields were moderate and the method involved tedious experimental procedure. Improvement in yields of monoacetylation was required. Here we report the facile preparation of monoacetates of symmetrical diols using HY-Zeolite as a catalyst (Scheme 1).

Reactions carried out under heterogeneous catalysis have recently gained increasing attention because of the use of inexpensive and non-corrosive catalysts, highly efficient transformations, easy experimental procedures and high purity of the products. Several heterogeneous catalysts have now been introduced to perform various chemical transformations.[11] Acidic zeolites are important and useful heterogeneous catalysts due to the ease of their separation, their reusability and ability to carry out the transformations with higher yields and selectivity than when homogeneous catalysts are used.[12] We have recently observed that HY-Zeolite is an efficient heterogeneous catalyst for the preparation of monoacetylated symmetrical diols.

Several symmetrical diols were treated with HOAc for 2–6 hours in the presence of HY-Zeolite under refluxing conditions. The monoacetates of the diols were formed in high yields (Table 1).

Using HOAc as acetylating agent no diacetates could be detected under the reaction conditions. However, acetylation with Ac_2O afforded a little diacetate (7–12%) along with monoacetate (75–80%) in each case.[3] Moreover, from an industrial point of view, anhydrides are more expensive than the corresponding carboxylic acids. Transesterification of diols with EtOAc was also achieved by heating under reflux (3.5–8.0 h) with HY-Zeolite. In this case the monoacetates were also produced selectively.[4] This method is of particular convenience since the reacting ester (EtOAc) is readily available and is also used as the solvent. Corrosive acetylating reagents are avoided and the reaction work up is very simple. However, the yields of the products were somewhat lower and the times of conversion somewhat longer than when HOAc was employed (Table 1).



Scheme 1

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Table 1 Preparation of Monoacetates of Symmetrical Diols

Entry	Diol	Acetylating agent	Time (h)	Isolated Yield (%)
	$HO(CH_2)_nOH$			
1	n = 2	HOAc	2	90
		EtOAc	3.5	83
2	n = 3	HOAc	2	89
		EtOAc	3.5	82
3	n = 4	HOAc	3	98
		EtOAc	5	91
4	n = 5	HOAc	3	95
		EtOAc	5	86
5	n = 6	HOAc	3.5	96
		EtOAc	5.5	87
6	n = 8	HOAc	3.5	93
		EtOAc	6	84
7	n = 9	HOAc	3.5	92
		EtOAc	6	81
8	n = 10	HOAc	4	94
		EtOAc	7	85
9	n = 12	HOAc	4.5	95
		EtOAc	7	81
10	n = 16	HOAc	6	92
		EtOAc	8	78
11	$HOCH_2CH=CHCH_2OH$	HOAc	3.5	93
		EtOAc	5	85
12	$HOCH_2C\equiv CCH_2OH$	HOAc	4	92
		EtOAc	5.5	83

The structures of the products were confirmed from spectral (IR, ^{1}H NMR and MS) data.

The monoacetates of symmetrical diols were also prepared by selective monodeacetylation of diacetates by heating under reflux (2.5–6.5 h) with commercial MeOH over HY-Zeolite (Table 2). The yields of the monoacetates were very high. The structures of the products were confirmed from their spectral (IR, ^{1}H NMR and MS) data.

The scope and limitation of the developed methodology have been studied. Carbon-Carbon multiple bonds present in the symmetrical diols are unaffected during acetylation of the compounds or deacetylation of the corresponding diacetates (Tables 1 and 2). Several 2-oxy-derivatives of 1,2,3-propane triol (**I**) were acetylated with HOAc or EtOAc. Alkyl ethers (like MeO, EtO, BnO) were unchanged under the present experimental conditions to yield the corresponding monoacetates in high yields (81–87%). However, compound **I** (Figure 1) with Me_3Si ether group afforded a mixture of products.

Table 2 Selective Monodeacetylation of Symmetrical Diacetates

Entry	Diacetate	Time (h)	Isolated Yield%
	$AcO(CH_2)_nOAc$		
1	n = 2	2.5	88
2	n = 3	2.5	85
3	n = 4	3	97
4	n = 5	3	93
5	n = 6	3.5	96
6	n = 8	4	94
7	n = 9	4	91
8	n = 10	4.5	93
9	n = 12	5	91
10	n = 16	6.5	90
11	$AcOCH_2CH=CHCH_2OAc$	4.5	93
12	$AcOCH_2C\equiv CCH_2OAc$	5	92

The structures of the products were confirmed from spectral (IR, ^{1}H NMR and MS) data.

The present methodology was again examined with symmetrical secondary and tertiary diols. The yields of monoacetates obtained either directly by acetylation of the symmetrical secondary diols (**II**) (Figure 1) or by deacetylation of the corresponding diacetates using HY-Zeolite were found to be poor (33–41%). On the other hand, symmetrical tertiary diols did not afford any acetylated product. Some unsymmetrical substituted 1,2-diols (**III**) (Figure 1) were also studied. Acetylation of the compounds under the described conditions (5–7.5 h) produced only the monoacetates formed by acetylation of the primary hydroxyl group. Thus the present method offers excellent selectivity for protection of primary hydroxyl group in the presence of secondary hydroxyl group.

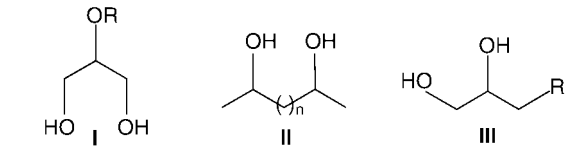

Figure 1

The catalyst HY-Zeolite is non-hazardous and environmentally benign. It can easily be removed from the reaction mixture by simple filtration. Acetylation of alcohols

can be achieved by treatment with carboxylic acids in the presence of a conventional Lewis acid but the catalyst is destroyed in the work-up procedure. We have observed that HY-Zeolite can be reused at least three times without losing its activity. The process is thus economic. The catalyst is commercially available (PQ Corporation, USA). It has the following physico-chemical parameters: Si/Al, 2.6 and surface area, 457.19 m^2/g. The experimental procedures for both the monoacetylation of symmetrical diols and monodeacetylation of symmetrical diacetates using this catalyst are very simple. The catalytic activity of HY-Zeolite is independent of the length of the diols.

In conclusion, we have developed a novel practical method for the preparation of monoacetates of saturated and unsaturated symmetrical diols starting from the diols themselves or from their diacetates in the presence of HY-Zeolite as a convenient and efficient catalyst. The operational simplicity, high yields of the products, high selectivity and reusable property of the catalyst are the advantages of the present protocol. We feel the developed method is an attractive alternative to the existing processes for the selective preparation of monoacetates of symmetrical diols.

Treatment of Diols with HOAc: Dodecane-1,12-diol (Table 1, entry 9) (202 mg, 1 mmol) was dissolved in HOAc (0.5 mL). HY-Zeolite (PQ Corporation, USA) (150 mg) and $CHCl_3$ (8 mL) were added. The mixture was heated under reflux for 4.5 h, cooled and filtered. The organic layer was washed with 5% Na_2CO_3 (3×5 mL), the solvent was evaporated and the residue subjected to purification by column chromatography over silica gel to afford 12-acetoxy dodecane-1-ol as a white solid (232 mg, 95%). IR (KBr): 3286, 1742, 1398, 1239, 1052 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): $\delta = 4.02$ (t, $J = 7.0$ Hz, 2 H), 3.54 (t, $J = 7.0$ Hz, 2 H), 2.00 (s, 3 H), 1.56–1.42 (m, 4 H), 1.34–1.18 (m, 16 H). FABMS: $m/z = 244$ [M^+].

Treatment of Diols with EtOAc: Decane-1,10-diol (Table 1, entry 8) (174 mg, 1 mmol) was dissolved in EtOAc (8 ml). HY-Zeolite (150 mg) was added to the solution and the mixture was heated under reflux for 7 h. After filtration of the catalyst the reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography over silica gel to produce 10-acetoxy decane-1-ol as a white solid (183 mg, 85%). IR (KBr): 3442, 1745, 1365, 1240, 1041 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): $\delta = 4.04$ (t, $J = 7.0$ Hz, 2 H), 3.60 (t, $J = 7.0$ Hz, 2 H), 2.03 (s, 3 H), 1.64–1.46 (m, 4 H), 1.42–1.22 (m, 12 H). FABMS: $m/z = 216$ [M^+].

Treatment of Diacetates with MeOH: 1,6-Diacetoxyhexane diacetate (Table 2, entry 5) (202 mg, 1 mmol) was dissolved in commercial MeOH (10 mL). HY-Zeolite (150 mg) was added. The mixture was heated under reflux for 3.5 h and after cooling this was filtered. The filtrate on concentration afforded a residue, which on purification by column chromatography over silica gel yielded 6-acetoxy hexane-1-ol as a colorless viscous mass (154 mg, 96%). IR (neat): 3428, 1744, 1336, 1047 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): $\delta = 4.05$ (t, $J = 7.0$ Hz, 2 H), 3.55 (t, $J = 7.0$ Hz, 2 H), 2.02 (s, 3 H), 1.62–1.44 (m, 4 H), 1.42–1.26 (m, 4 H). FABMS: $m/z = 160$ [M^+].

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